UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: 16 JULY 2004

SUBJECT: **SPINOSAD -** Exposure/Risk Assessment of the Insecticide Spinosad Used as a Stored Grain Protectant

PC Code: 110003 DP Code: 304201

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INTRODUCTION

Dow AgroSciences has requested Section 3 registration under the Federal Fungicide, Insecticide and Rodenticide Act, as amended of the compound spinosad for use as a protectant of stored grain. Grains listed on the proposed label are barley, birdseed, corn, cotton seed, oats, peanuts (in shell), rice, sorghum/milo, soybeans, sunflower and wheat. The products proposed for use are Entrust® (EPA Reg. No. 62719 - 282) which is an 80 % wettable powder and NAF - 313 (EPA Reg. No. 62719 - 291) which is a 1.0 lb active ingredient per gallon liquid soluble concentrate. This memorandum serves as HED's assessment of occupational pesticide handler exposure and risk from the proposed new uses.

USE PATTERN SUMMARY

Spinosad in either formulation would be applied to prevent damage to stored grain (noted above) from grain insect pests including the lesser grain borer, Indian meal moth, Angoumois grain moth, rice weevil, granary weevil, maize weevil, red-flour beetle, saw-toothed grain beetle, flat

grain beetle. The rates of application vary from 0.64 dry oz. Entrust® (0.032 lb a.i.) per 1,000 bushels to 1.20 dry oz. Entrust® (0.06 lb a.i.) per 1,000 bushels depending upon grain species.

NAF - 313 rates of application vary from 4.0 fl oz (0.03125 lb a.i.) per 1,000 bushels to 7.8 fl oz (0.061 lb a.i.) per 1,000 bushels depending upon species of grain. One application is permitted. Spinosad will be applied as a coarse spray to the grain "stream" as it is augered or conveyed to a silo or similar storage facility. See Table 1.0 for a summary of the proposed use pattern.

Table 1.0 Summary of Proposed Use Pattern for Spinosad as a Stored Grain Protectant

Crop Site	stored grain: barley, birdseed, corn, cotton seed, oats, peanuts (in shell), rice, sorghum/milo, soybeans, sunflower, wheat
Pest	lesser grain borer, Indian meal moth, Angoumois grain moth, rice weevil, granary weevil, maize weevil, red-flour beetle, saw-toothed grain beetle, flat grain beetle.
Formulation	Entrust® (EPA Reg. No. 62719 - 282) an 80 % wettable powder and NAF - 313 (EPA Reg. No. 62719 - 291) a 1.0 lb active ingredient per gallon liquid soluble concentrate.
Application Method	coarse spray to grain "stream" as augered or conveyed
Application Rate	0.031 - 0.061 lb a.i./1,000 bushels
Application Number	1 application
Restricted Entry Interval	4 hours
Manufacturer	Dow AgroSciences

OCCUPATION PESTICIDE HANDLER

For the proposed use pattern, HED believes that the individual who prepares the spray mixture (i.e, mixer/loader) is essentially the only person exposed. There is no "applicator" *per se* and "applicator" exposure was not assessed. Once the spray mixture is prepared, the spray is applied to the grain stream from nozzles mounted above an auger or conveyer as the grain is lifted into a silo or other storage facility. Further, HED believes that the mixer/loader (i.e., the applicator) will be exposed over short-term (1 - 30 days) durations. Based on communications with experts in the field of stored grain protection, up to 250,000 bushels of grain may be lifted into a silo per day during the harvest season. HED uses that figure as the basis of its estimate of handler exposure.

Chemical specific data were not available with which to assess pesticide handler exposure. Therefore surrogate data from studies in the Pesticide Handler Exposure Database Version 1.1 (August 1998) PHED SURROGATE EXPOSURE GUIDE were used to estimate handler

(mixer/loader) exposure.

It is HED policy to assess handler exposure and risk using "baseline" personal protective equipment (PPE) which is comprised of long sleeved shirt, long pants, and shoes plus socks and to assess "baseline" **plus the use of protective gloves** or other PPE as might be necessary or appropriate. The proposed labels direct pesticide handlers to wear a long sleeved shirt, long pants and shoes plus socks.

On 11 July 2002, the HED Hazard Identification Assessment Review Committee (HIARC) met to discuss the adequacy of the toxicological database relative to the compound spinosad. Relevant to the assessment herein, the HIARC **did not** identify dermal toxicological endpoints. The HIARC cited the "1) lack of appropriate endpoints; 2) the combination of molecular structure and size as well as the lack of dermal or systemic toxicity at 2,000 mg/kg (acute dermal toxicity study) and at 1,000 mg/kg/day in a 21-day dermal toxicity study in rats which indicates the lack of dermal absorption; and 3) the lack of long-term exposure based on the current use pattern."

However, the HIARC did identify a short-term (1 - 30 days) inhalation toxicological endpoint. The No Observable Adverse Effect Level (NOAEL) is 4.9 mg a.i./kg bw/day and the endpoints (effects seen) were microscopic changes in multiple organs, clinical signs of toxicity, decreases in mean body weights and food consumption and biochemical evidence of anemia and possible liver damage. A Margin of Exposure (MOE) $\geq$ 100 is adequate to protect occupational pesticide handlers from exposures to spinosad. The HIARC classified spinosad as "not likely" to be a human carcinogen therefore a cancer risk assessment is not necessary. See the ATTACHMENT for a summary of the toxicological endpoints for use in risk assessment. See Table 2.0 for a summary of exposures and risks to pesticide handlers.

Table 2.0 Estimated Handler Exposure and Risk from the Use of Spinosad as a Stored Grain Protectant						
Unit Exposure[1] mg a.i./lb handled		**Applic. Rate[2]**	**Units Treated[3]** Per Day	**Average Daily Dose[4] mg a.i./kg bw/day**	**NOAEL[5] mg a.i./kg bw/day**	**MOE[6]**
Mixer/Loader - Liquid - Open Pour						
Inhal	0.0012 HC	0.061 lb a.i./1,000 bushels	250,000 bushels/day	Inhal 0.000261	4.9	18,774
Mixer/Loader - Wettable Powder - Open Bag						
Inhal	0.0043 MC	0.061 lb a.i./1,000 bushels	250,000 bushels/day	Inhal 0.000937	4.9	5,229

1. Unit Exposures are taken from "PHED SURROGATE EXPOSURE GUIDE", Estimates of Worker Exposure from The Pesticide Handler Exposure Database Version 1.1, August 1998. Inhal. = Inhalation. Units = mg a.i./pound of active ingredient handled. Data Confidence: LC = Low Confidence, MC = Medium Confidence, HC = High Confidence.
2. Applic. Rate. = Taken from Entrust® and NAF - 313 labels (62719 - 282 and 62719 - 291 respectively)
3. Units Treated are taken from communications with stored grain expert.
4. Average Daily Dose(ADD) = Unit Exposure * Applic. Rate * Units Treated ÷ Body Weight (70 kg).
5. MOE = Margin of Exposure = No Observable Adverse Effect Level (NOAEL) ÷ ADD. Short-term inhalation NOAEL = 4.9 mg a.i./kg bw/day identified from a subchronic feeding study in the dog.

A MOE of 100 is adequate to protect occupational pesticide handlers. Since the calculated MOEs are > 100, the proposed use does not exceed HED's level of concern.

POST-APPLICATION EXPOSURE

Typical post-application exposure is not expected since there are no crop advisors or agricultural workers. Treated grain is stored in silos or similar facilities and therefore not "entered" as one might for row crops or other agricultural uses. If stored grain were to be inspected, HED believes any inhalation exposure would be negligible and would certainly be less than what has been estimated for the mixer/loaders as presented above. Therefore, the proposed use does not exceed HED's level of concern.

RESTRICTED ENTRY INTERVAL (REI)

Spinosad is classified in acute dermal toxicity category III and toxicity category IV for acute inhalation, primary eye irritation and primary skin irritation. It is not a dermal sensitizer. Spinosad has a REI of four (4) hours.

ATTACHMENT

Acute Toxicity of Spinosad

Guideline No.	Study Type	MRID #(s)	Results	Toxicity Category
81-1	Acute Oral-Rat	43770701 43414515	LD_{50} = >2000 mg/kg	III
81-2	Acute Dermal-Rabbit	43414516	LD_{50} = >2000 mg/kg	III
81-3	Acute Inhalation-Rat	43414517	LC_{50} = >5.18 m/L	IV
81-4	Primary Eye Irritation	43414518	not an eye irritant	IV
81-5	Primary Skin Irritation	43414519	not a skin irritant	IV
81-6	Dermal Sensitization	43414520	not a skin sensitizer	n/a

Summary of Toxicology Endpoint Selection for Spinosad

Exposure Scenario	**Dose (mg/kg/day) UF /MOE**	**Hazard Based Special FQPA Safety Factor**	**Endpoint for Risk Assessment**
Dietary Risk Assessments			
Acute Dietary females 13-50 years of age	NOAEL = N/A UF = N/A **Acute RfD** = N/A mg/kg/day	N/A	**[N/A]** LOAEL = **[N/A]** mg/kg/day based on **[N/A]**. No endpoint attributable to a single exposure was identified. This risk assessment is not required.
Acute Dietary general population including infants and children	NOAEL = **[N/A]** UF = **[N/A]** **Acute RfD** = **[N/A]** mg/kg/day	N/A	**[N/A]** LOAEL = **[N/A]** mg/kg/day based on **[N/A]** No endpoint attributable to a single exposure was identified for the general population, including infants and children. This risk assessment is not required.

Exposure Scenario	Dose (mg/kg/day) UF /MOE	Hazard Based Special FQPA Safety Factor	Endpoint for Risk Assessment
Chronic Dietary <u>all populations</u>	NOAEL= **2.7** UF = **100** **Chronic RfD** = **0.027** mg/kg/day	1x	**[Chronic Toxicity Study in Dogs]** LOAEL = **[8.22]** mg/kg/day based on vacuolation in glandular cells (parathyroid) and lymphatic tissues, arteritis, and increases in serum alanine aminotransferase, aspartate aminotransferase, and triglycerides levels
Incidental Oral Short-Term (1 - 30 Days) Residential Only	NOAEL= **4.9** mg/kg/day **MOE= 100**	1x	**[Subchronic Feeding Study in Dogs]** LOAEL = **[9.73]** mg/kg/day based on microscopic changes in a multiple organs, clinical signs of toxicity, decreases in mean body weights and food consumption and biochemical evidence of anemia and possible liver damage
Incidental Oral Intermediate-Term (1 - 6 Months) Residential Only	NOAEL= **2.7** mg/kg/day **MOE = 100**	1x	**[Chronic Toxicity Study in Dogs]** LOAEL = **[8.22]** mg/kg/day based on vacuolation in glandular cells (parathyroid) and lymphatic tissues, arteritis, and increases in serum alanine aminotransferase, aspartate aminotransferase, and triglycerides levels
Non-Dietary Risk Assessments			

Exposure Scenario	Dose (mg/kg/day) UF /MOE	Hazard Based Special FQPA Safety Factor	Endpoint for Risk Assessment
Dermal Short-Term (1 - 30 days)	NOAEL= **N/A**	N/A	Short-,Intermediate-and Long-Term dermal risk assessments because: 1) lack of appropriate endpoints; 2) the combination of molecular structure and size as well as the lack of dermal or systemic toxicity at 2000 mg/kg (acute dermal toxicity study) and at 1000 mg/kg/day in a 21-day dermal toxicity study in rats which indicates the lack of dermal absorption; and 3) the lack of long-term exposure based on the current use pattern. **Dermal risk assessment is not required.**
Residential	**MOE = N/A**	N/A	
Occupational	N/A	N/A	
Dermal Intermediate-Term (1 - 6 Months)	NOAEL= **N/A**	N/A	Short-,Intermediate-and Long-Term dermal risk assessments because: 1) lack of appropriate endpoints; 2) the combination of molecular structure and size as well as the lack of dermal or systemic toxicity at 2000 mg/kg (acute dermal toxicity study) and at 1000 mg/kg/day in a 21-day dermal toxicity study in rats which indicates the lack of dermal absorption; and 3) the lack of long-term exposure based on the current use pattern. **Dermal risk assessment is not required.**
Residential	**MOE = N/A**	N/A	
Occupational	N/A	N/A	

Exposure Scenario	Dose (mg/kg/day) UF /MOE	Hazard Based Special FQPA Safety Factor	Endpoint for Risk Assessment
Dermal Long-Term (> 6 Months)	NOAEL= **N/A**	N/A	Short-,Intermediate-and Long-Term dermal risk assessments because: 1) lack of appropriate endpoints; 2) the combination of molecular structure and size as well as the lack of dermal or systemic toxicity at 2000 mg/kg (acute dermal toxicity study) and at 1000 mg/kg/day in a 21-day dermal toxicity study in rats which indicates the lack of dermal absorption; and 3) the lack of long-term exposure based on the current use pattern. **Dermal risk assessment is not required.**
Residential	**MOE = N/A**	N/A	
Occupational	N/A	N/A	
Inhalation Short-Term (1 - 30 days)	Oral NOAEL= **4.9** mg/kg/day	1x	**[Subchronic Feeding Study in Dogs]** LOAEL = **[9.73]** mg/kg/day based on microscopic changes in a multiple organs, clinical signs of toxicity, decreases in mean body weights and food consumption and biochemical evidence of anemia and possible liver damage
Residential	**MOE = 100**	1x	
Occupational	100	1x	
Inhalation Intermediate-Term (1 - 6 Months)	Oral NOAEL= **2.7** mg/kg/day	1x	**[Chronic Toxicity Study in Dogs]** LOAEL = **[8.22]** mg/kg/day based on vacuolation in glandular cells (parathyroid) and lymphatic tissues, arteritis, and increases in serum alanine aminotransferase, aspartate aminotransferase, and triglycerides levels
Residential	**MOE = 100**	1x	
Occupational	100	1x	
Inhalation Long-Term (>6 Months)	Oral NOAEL= 2.7 mg/kg/day	1x	**[Chronic Toxicity Study in Dogs]** LOAEL = **[8.22]** mg/kg/day based on vacuolation in glandular cells (parathyroid) and lymphatic tissues, arteritis, and increases in serum alanine aminotransferase, aspartate aminotransferase, and triglycerides levels

Exposure Scenario	Dose (mg/kg/day) UF /MOE	Hazard Based Special FQPA Safety Factor	Endpoint for Risk Assessment
Residential	**MOE = 100**	1x	
Occupational	100	1x	
Cancer	**Classification: Not likely to be carcinogen** **Q1*** = N/A		

Use 100% inhalation absorption factors to inhalation risk assessments when an oral NOAEL is selected.
TBD = To Be Determined. Target MOEs for residential exposures will be determined by the FQPA Safety Factor Committee. The FQPA SFC recommended that the FPQA Safety Factor be removed (HED Doc. No. 013341).

Attachment taken from Memo, P. Shah, 11 July 2002, "SPINOSAD - 2nd Report of the Hazard Identification Assessment Review Committee." PC Code 110003.

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